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Invited Commentary

Invited Commentary: Personality as a Causal Factor in Cancer Risk and Mortality—Time to Retire a Hypothesis?

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In this issue of the *Journal*, Nakaya et al. (*Am J Epidemiol.* 2010;172(4):377–385) report null findings from a large-scale prospective study of the prognostic value of 2 personality dimensions, neuroticism and extraversion, for cancer risk and mortality. The study stands out because of its exceptionally large sample size and its methodological strengths. The authors discuss the Nakaya et al. study in the context of persistent beliefs about the role of personality in cancer onset and survival despite a pattern of null findings in the literature, as well as the influence of extreme outlier findings from one investigator group that continue to be cited. They question whether it is time for the field to move on from considering a role for personality in cancer to more promising and modifiable factors.

extraversion (psychology); neoplasms; personality; personality inventory; psychology; risk factors; stress (psychological); survival

Is it finally time to retire the hypothesis that personality is a significant causal factor in cancer? The hypothesis can be traced to the writings of Hippocrates and Galen, but, in modern times, it has become embedded in a matrix of strongly held cultural beliefs about mind-body relations, including beliefs that personality traits such as optimism and fighting spirit can not only promote the psychological adjustment of persons diagnosed with cancer but also extend their survival. Seemingly extraneous factors such as culture and ideology are needed to explain the persistence of the hypothesis in the face of a pattern of mostly null findings from a generally poor-quality literature with a documented publication bias (1), as well as the influence of some data of dubious validity. This is buoyed by the support of extreme outlier findings from one investigator group of a strong association that continue to be cited, despite being generally regarded by some as too good to be true.

It is in this context that the results of the Nakaya et al. study (2) will be interpreted. These investigators present basically null results from an exceptionally large, population-based, prospective cohort study that raise questions as to whether it might be time to reevaluate whether there is any credible evidence for a role of personality in cancer incidence and survival and, furthermore, whether it is reasonable to expect that any revision of a negative assessment of the current

available literature will be likely based on data not yet available. Could it be time to stop looking for an association between personality and cancer and turn our attention to larger, more robust and potentially modifiable factors for cancer risk and mortality?

Using what is undoubtedly the largest relevant data set ever assembled, Nakaya et al. (2) report the prognostic value of 2 personality dimensions, neuroticism and extraversion, for cancer risk and mortality. The data were derived from persons in a Finnish same-sex twin registry (31,145 persons) and a Swedish twin registry (36,336 persons) who completed a baseline personality questionnaire and were followed up for a maximum of 30 years. Data concerning incidence and survival for all cancers and for as many as 13 specific cancer sites were derived from cancer registries and population registries. More than 4,500 incident cases of cancer and more than 1,500 cancer-related deaths were recorded in the observation period.

Results are simply summarized: unadjusted analyses revealed no association for either neuroticism or extraversion with all-cancer incidence and mortality. Yet, findings from unadjusted analyses revealed a positive association with incident lung cancer that persisted after adjustments for possible confounders and mediating pathways, and a negative association for liver cancer that persisted after similar

adjustment for covariates. In terms of cancer survival, both unadjusted and multivariate analyses found no prognostic value of personality for any specific cancer site.

The care with which analyses were conducted and interpreted is noteworthy, particularly given the limitations of the existing literature. Analyses were stratified by country and gender. Adjustments were made for possible dependence among twins, and time since baseline personality assessment was entered as a time-dependent variable. A role for zygosity was examined and rejected, thus addressing more general concerns about the study having relied on twins and possibly having introduced the complications of genetic influences on personality. Overall incidence of cancer and cancer mortality was adequate for all-cancer analyses, and analyses for specific sites were restricted to those cancers for which there were at least 100 incident cases.

Moreover, better-nuanced smoking data available for the Swedish subsample allowed examination of whether the association between personality might further be reduced when moving from a dichotomous indicator of smoking status to a 4-level indicator. The already small association persisted, but its reduction led investigators to infer that better assessment of smoking status and exposure might eliminate the association altogether. It is noteworthy that no plausible biologic pathway can be mustered to explain an approximately small, similarly sized, *reduced* risk of liver cancer associated with personality. Unless we are willing to fall prey to a confirmatory bias already pervasive in this literature, we might concede that both are due to chance rather than embrace one finding but not the other.

The Nakaya et al. study (2) corroborates findings on the role of personality from other prospective studies but contrasts with findings from studies of poorer quality (3). Studies have sometimes been underpowered to the extent that use of multivariate techniques becomes problematic, risking spurious findings because of overfitting of regression equations (4). In this literature, there are few instances of data having been originally collected with a specific study of the personality-cancer link in mind, so assessment of covariates fundamental to evaluating confounders and mediators is generally inadequate, with covariates limited to whatever variables happened to have been collected for other purposes. Still, there often seems to be little rationale for using particular variables and not others as covariates in these studies, except that they were available or survived some preselection process, and interpretation of results typically does not consider the distinction between a confounder and a mediator. In their study, Nakaya et al. clearly distinguished between confounders and possible pathways, importantly considering smoking as a possible pathway to explain the few significant associations they found. In doing so, this study is one of the few, if not the only one, even beginning to test the role of personality as a causal factor for cancer by including meaningful potential pathways.

Previous reviews concur that there is no convincing evidence for the role of personality in cancer development (3, 5, 6). Prospective studies with large sample sizes sometimes find results that are significant, but the magnitude of the association is generally low. One recent, comprehensive meta-analytic review (1) did report an unexpectedly high

hazard ratio of 1.29 (95% confidence interval: 1.16, 1.44) for stress-related factors, including personality, associated with mortality from cancers. However, as we have argued elsewhere (7), this hazard ratio was influenced by inclusion of the work of Grossarth-Maticek et al. (8–10). This work was severely criticized and was excluded for this reason from another systematic review that examined the effects of psychosocial interventions on survival (11).

The study of Nakaya et al. (2) assessed personality with an instrument developed by Hans Eysenck. The personality measure is well validated and widely accepted, but Eysenck's views on the relation of personality to cancer are not. Eysenck was one of the most vigorous proponents of personality as a risk factor for cancer, postulating that personality was both a psychological stress diathesis and a stress generator (12, 13). Eysenck argued that, as a risk factor for lung cancer, personality was stronger than smoking and that, in fact, any apparent association between smoking and lung cancer was spurious, with personality being related to both smoking and lung cancer but smoking not being directly related to lung cancer. The evidence that Eysenck mustered for these claims drew heavily on the aforementioned work of Grossarth-Maticek et al. (8–10), with whom he coauthored a number of papers (9, 10). These studies tested the presumed role of personality in cancer mortality, which resulted in extremely strong hazard ratios, ranging from 23.8 to 74.2, which stand in sharp contrast to hazard ratios for personality that barely exceed 1 (3). To our knowledge, these findings are without precedent and have not been replicated by other investigator groups. Moreover, the studies were severely criticized because of suspected manipulations and inconsistencies in the information regarding the realization of the studies and the outright improbability that data could have been collected as reported (14–16).

Given the doubts raised about the validity of the Grossarth-Maticek studies (8–10), it is remarkable that they continue to be included in and hence influence outcomes of systematic reviews (1) and to be cited without expression of doubt or caution about their interpretation (17–19), and so they remain influential in direct and indirect ways. A recent study of stress and breast cancer incidence by Michael et al. (19) drawing on Women's Health Initiative data is framed in terms of theoretical models "based on extensive biological data" suggesting complex links between stress and cancer risk. The particular model cited (20) depends heavily on data from Grossarth-Maticek and Eysenck, some of which Michael et al. cite. Despite elaborate parsing and analysis of their data, Michael et al. were left with essentially null findings. They conceded that evidence for a role of stress in breast cancer incidence is weak, but they nonetheless asserted that evidence for a role of stress in cancer progression and outcome has been "convincingly demonstrated." Overall, this paper (19) illustrates how the work of Grossarth-Maticek and Eysenck continues to be influential and uncritically quoted and is suggestive of how the publication bias that has been noted in this literature occurs.

One reason for continued interest in what is generally found to be a weak association between psychological factors and cancer onset and survival in general is that faith in

this association can be cited as the rationale for programs of research investigating the promise that altering psychological states might affect cancer progression and, ultimately, survival of cancer patients (21). Yet, the evidence concerning the effectiveness of psychological interventions in affecting cancer survival is remarkably consistent: no intervention study in which survival was an a priori endpoint and in which there was adequate control of medical cotreatment confounding has ever found an effect (22).

Could it be time that the null results of Nakaya et al.'s study (2) be given a weight that takes into account not only the study's superior sample size but also its methodological strengths? Residual confounding may never totally be eliminated, but we now can be reasonably confident that the overall effect size for a personality-cancer causal association is much too small to have clinical and public health implications, if it exists at all. Will the hypothesis of a link be retired or simply quietly pass into oblivion? Disappearance will probably not be the case because of the congruence with strongly held cultural beliefs and ideology. If the question can be presumed to still be open regarding psychological vulnerability to stress—notably, personality and its presumed effect on cancer risk and survival—interest and investment in this broader hypothesis will be rendered only when high-quality studies including standards similar to those set by Nakaya et al. (2) are conducted.

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REFERENCES

- Chida Y, Hamer M, Wardle J, et al. Do stress-related psychosocial factors contribute to cancer incidence and survival? *Nat Clin Pract Oncol*. 2008;5(8):466–475.
- Nakaya N, Bidstrup PE, Saito-Nakaya K, et al. Personality traits and cancer risk and survival based on Finnish and Swedish registry data. *Am J Epidemiol*. 2010;172(4):377–385.
- Ranchor AV, Sanderman R. The role of personality in cancer onset and survival. In: Vollrath ME, ed. *Handbook of Personality and Health*. Hoboken, NJ: John Wiley & Sons; 2006:36–49.
- Babyak MA. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. *Psychosom Med*. 2004;66(3):411–421.
- Garssen B. Psychological factors and cancer development: evidence after 30 years of research. *Clin Psychol Rev*. 2004;24(3):315–338.
- Petticrew M, Bell R, Hunter D. Influence of psychological coping on survival and recurrence in people with cancer: a systematic review. *BMJ*. 2002;325(7372):1066–1069.
- Coyne JC, Ranchor AV, Palmer SC. Meta-analysis of stress-related factors in cancer. *Nat Rev Clin Oncol*. 2010;7(5):1–2.
- Grossarth-Maticek R, Bastiaans J, Kanazir DT. Psychosocial factors as strong predictors of mortality from cancer, ischaemic heart disease and stroke: the Yugoslav Prospective Study. *J Psychosom Res*. 1985;29(2):167–176.
- Grossarth-Maticek R, Eysenck HJ, Vetter H. Personality type, smoking habit and their interaction as predictors of cancer and coronary heart disease. *Pers Individ Dif*. 1988;9:479–495.
- Grossarth-Maticek R, Eysenck HJ, Pfeifer A, et al. The specific action of different personality risk factors on cancer of the breast, cervix, corpus uteri and other types of cancer: a prospective investigation. *Pers Individ Dif*. 1997;23(6):949–960.
- Smedslund G, Ringdal GI. Meta-analysis of the effects of psychosocial interventions on survival time in cancer patients. *J Psychosom Res*. 2004;57(2):123–131; discussion 133–135.
- Eysenck HJ. The respective importance of personality, cigarette-smoking and interaction effects for the genesis of cancer and coronary heart disease. *Pers Individ Dif*. 1988;9:453–464.
- Eysenck HJ. The prediction of death from cancer by means of personality/stress questionnaire: too good to be true? *Percept Mot Skills*. 1990;71(1):216–218.
- Amelang M. Tales from Crvenka and Heidelberg: what about the empirical basis? *Psychol Inq*. 1991;2(3):233–236.
- Fox BH. Quandaries created by unlikely numbers in some of Grossarth-Maticek's studies. *Psychol Inq*. 1991;2(3):242–247.
- Van der Ploeg HM. What a wonderful world it would be: a reanalysis of some of the work of Grossarth-Maticek. *Psychol Inq*. 1991;2(3):280–285.
- Lehto US, Ojanen M, Dyba T, et al. Baseline psychosocial predictors of survival in localised breast cancer. *Br J Cancer*. 2006;94(9):1245–1252.
- Nabi H, Kivimäki M, Zins M, et al. Does personality predict mortality? Results from the GAZEL French prospective cohort study. *Int J Epidemiol*. 2008;37(2):386–396.
- Michael YL, Carlson NE, Chlebowski RT, et al. Influence of stressors on breast cancer incidence in the Women's Health Initiative. *Health Psychol*. 2009;28(2):137–146.
- Hilakivi-Clarke L, Clarke R, Lippman ME. Perinatal factors increase breast cancer risk. *Breast Cancer Res Treat*. 1994;31(2-3):273–284.
- Antoni MH, Lutgendorf S. Psychosocial factors and disease progression in cancer. *Curr Dir Psychol Sci*. 2007;16:42–46.
- Coyne JC, Stefanek M, Palmer SC. Psychotherapy and survival in cancer: the conflict between hope and evidence. *Psychol Bull*. 2007;133(3):367–394.